PROCEEDINGS
OF THE
NATIONAL ACADEMY OF SCIENCES
Volume 6 MAY 15, 1920 Number 5

CALCULATING ANCESTRAL INFLUENCE IN MAN

A MATHEMATICAL MEASURE OF THE DEMONSTRATED FACTS OF BI-SEXUAL HEREDITY

By Harry H. Laughlin

Eugenics Record Office, Carnegie Institution of Washington

Communicated by C. B. Davenport. Read before the Academy, November 10, 1919

By ancestral influence is meant the contribution of definite hereditary, mental, physical and moral qualities, by a given ancestor to a given descendant. Pedigree-studies have set forth in man, as in many other organisms, rules of inheritance of many specific traits or qualities. Cytological investigations have shown how chromosomes duplicate, segregate and recombine (sometimes crossing-over and showing other special phenomena) in the course of gametogenesis and fertilization.

In bi-sexual species of plants or animals, the germ-plasm is not indefinitely dilutable or divisible as many genealogists have assumed, but its dilutability and divisibility are limited by the number of chromosome-characteristics of the gametes of the particular species. In the human zygote two gametes each with 12 chromosomes unite. This means that, barring crossing-over, mutation and other special phenomena, normally the human germ-plasm, and consequently all hereditary human qualities, that is, the "blood," is divisible only into 24 unequal units corresponding to the 24 zygotic chromosomes.

Note—There is still disagreement among cytologists concerning the number of chromosomes in man.

Wieman, H. L., "The Chromosomes of Human Spermatocytes," *Amer. J. Anat.*, **21**, No. 1, January, 1917. This paper concludes that in man the zygotic or diploid number of chromosomes is 24, of which 2 are the *xy* idiochromosomes.

von Winiwarter, H., "Études sur la spermatogenèse humaine," *Arch. Biol.*, **27**, 1912. This paper concludes that the zygotic number of chromosomes in the human male is 47, in the human female, 48.

See also Stevens, Guyer, Montgomery and Evans.

When this problem is settled beyond peradventure, the correct number can be used in the accompanying formulas which are here stated in general terms.

It is well demonstrated that the chromosomes are composed of genes or the determiners of natural inheritance. Each chromosome is a gene-

radical or linkage-group of trait determiners. The chromosomes are the germ-plasm. If then it is sought to measure the influence of a given ancestor upon the hereditary traits of a given propositus, it is necessary to develop a series of mathematical formulas which measure the probabilities of definite situations happening in reference to the transmission of chromosomes from the given ancestor to the given propositus.

In developing such formulas the following factors must be taken into consideration:

First. Whether the species in question is bi-sexual.

Second. Whether in the particular species the male or the female is the heterozygous sex.

Third. Due provision must be made for sex-linked traits.

Fourth. The number of chromosomes, both gametic and zygotic, characteristic of the species, must be known.

Fifth. For the present the individual chromosomes will not be weighed, but simply counted. Doubtless the ontogenetic working out of each chromosome is very specific both qualitatively and quantitatively. When ultimately genetical and cytological research locate in definite chromosomes the genes for definite traits, then the several chromosomes can be weighted, and due provision for their differential values properly made in the formulas for measuring the several features of ancestral influence.

Sixth. Due cognizance must be taken of the possibility of mutation, crossing-over, non-disjunction and other special phenomena occurring in the course of the descent of chromosomes from a given ancestor to the propositus. In the accompanying formulas such phenomena are not provided for, because their rates of occurrence are not yet measurable in man, but when one by one their mathematical measures are attained, each such measure can be woven into the accompanying foundation formulas. The present formulas will not be upset by such corrections, but simply modified in the direction of greater accuracy.

Seventh. It must be considered that in a given gamete a definite chromosome may have been derived from either the paternal or the maternal source. This is especially important in cases of zygotes of mixed blood.

Eighth. In certain situations it will be necessary to specify whether a given trait is dominant or recessive to its allelomorph.

Finally, all formulas must be stated in general terms, so that they may apply with equal accuracy to any species concerning which chromosomal data are at hand.

There are many features of ancestral influence which may be mathematically formulated. Among them are (1) the average contribution in number of chromosomes that a given ancestor, taken as a type, will contribute to the propositus; (2) the range in such numbers; (3) the probability that the given ancestor, taken as a type, will contribute all of the hereditary influences which the particular half-pedigree furnishes to the

propositus; (4) the probability that the particular propositus, and consequently all of his or her direct ancestors, will be entirely eliminated as a contributor to the hereditary constitution of the propositus; (5) that a definite number of chromosomes specified as to maternity or paternity of origin, carried by a given ancestor, will by such ancestor be passed on to the propositus; (6) as one of many special cases, the probability that a given ancestor who appears once or more in each the maternal and paternal half-pedigree, will be duplicated exactly in zygotic chromosomal constitution by the propositus.

The principles set forth in the paper of which this is an abstract make possible the mathematical formulation of an indefinitely great number of complex situations in reference to ancestral influence. The completer paper presents in detail twenty-seven such formulas. Eight of these (numbers 1, 4, 5, 6, 7, 8, 9 and 10) for each individual pedigree-place, to which the particular formulas apply, were worked out for each member of the first five ancestral generations in man and shown on charts, entitled "Ancestral Influence in the Human Male," and "Ancestral Influence in the Human Female." (In the accompanying charts bearing the above titles these same formulas are worked out for the first three ancestral generations only.) These particular calculations in reference to man are based upon the following data and conditions: (*a*) that the gametic number of human chromosomes is 12; the zygotic or somatic number in each sex 24; (*b*) that the male is heterozygous (*xy*) and the female homozygous (*xx*) in reference to sex; (*c*) that all of the purely hereditary qualities are carried by the several chromosomes; and (*d*) that in the first or foundation formulas no provision will be made for mutation, crossing-over, non-disjunction or other special phenomena.

These eight formulas worked out in detail on the human pedigree-charts follow:

No. 1. A = Average number of chromosomes passed on by the selected ancestor, taken as a type, to the F_1 zygote, i. e., the propositus.

A = Also the average number of chromosome-pairs each of which contributes one member to the diploid or somatic group of chromosomes of the F_1 zygote.

In man the diploid or somatic number of chromosomes is taken tentatively at 24, i. e., 11 equivalent pairs and one *xx* or *xy* sex-pair.

$$A = \frac{n}{2^{(p-1)}} + \left\{ \begin{array}{l} (C_y \textit{ or } C_x \text{ in case of ancestors from whom an } x\text{- or a} \\ \qquad\qquad y\text{- chromosome } \textit{may} \text{ descend.}) \end{array} \right.$$

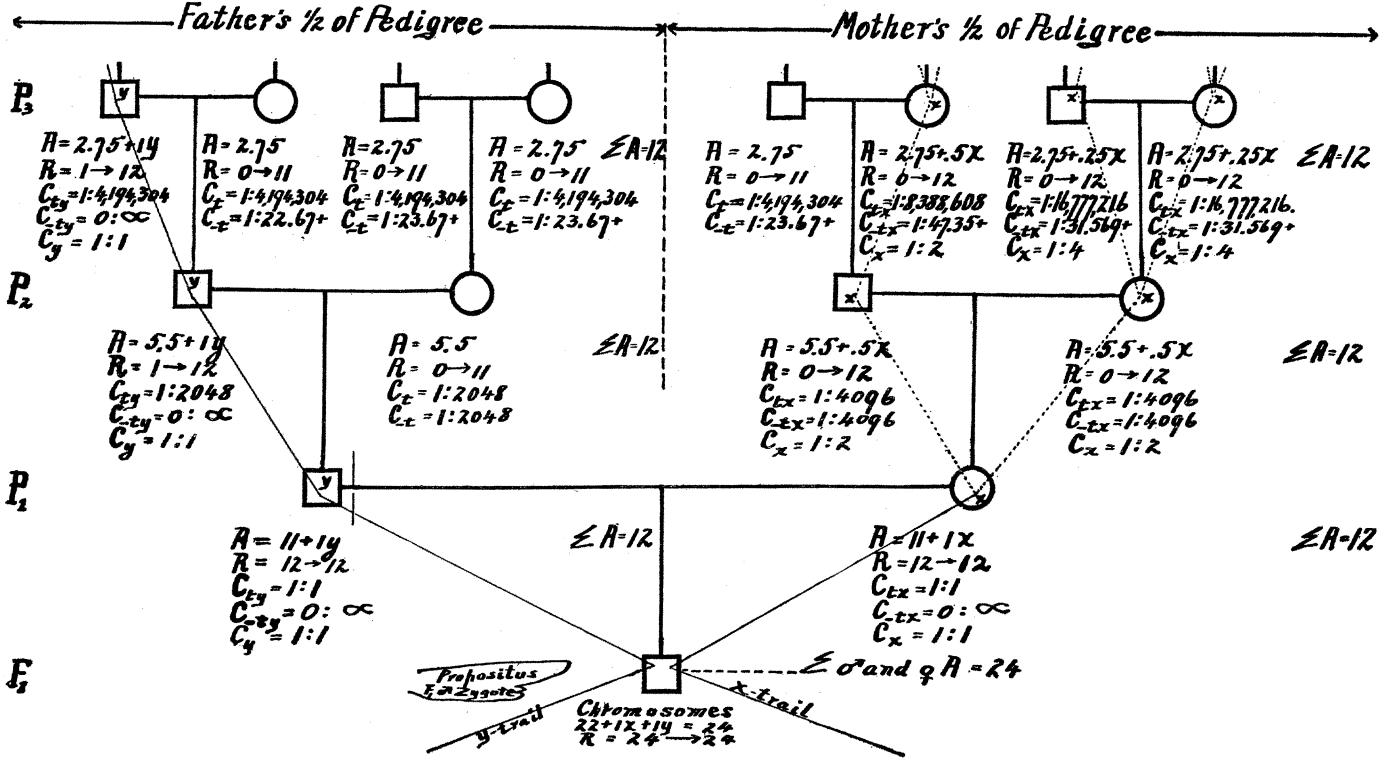
See notes on *x*- and *y*- trails, under formulas 4 and 5.

n = Number of equivalent chromosome-pairs (i. e., excluding the *xy* or the *xx* sex-pair) characteristic of the species. In man n is taken tentatively at 11.

p = the numerical value of the sub-figure of P used in pedigree-manner

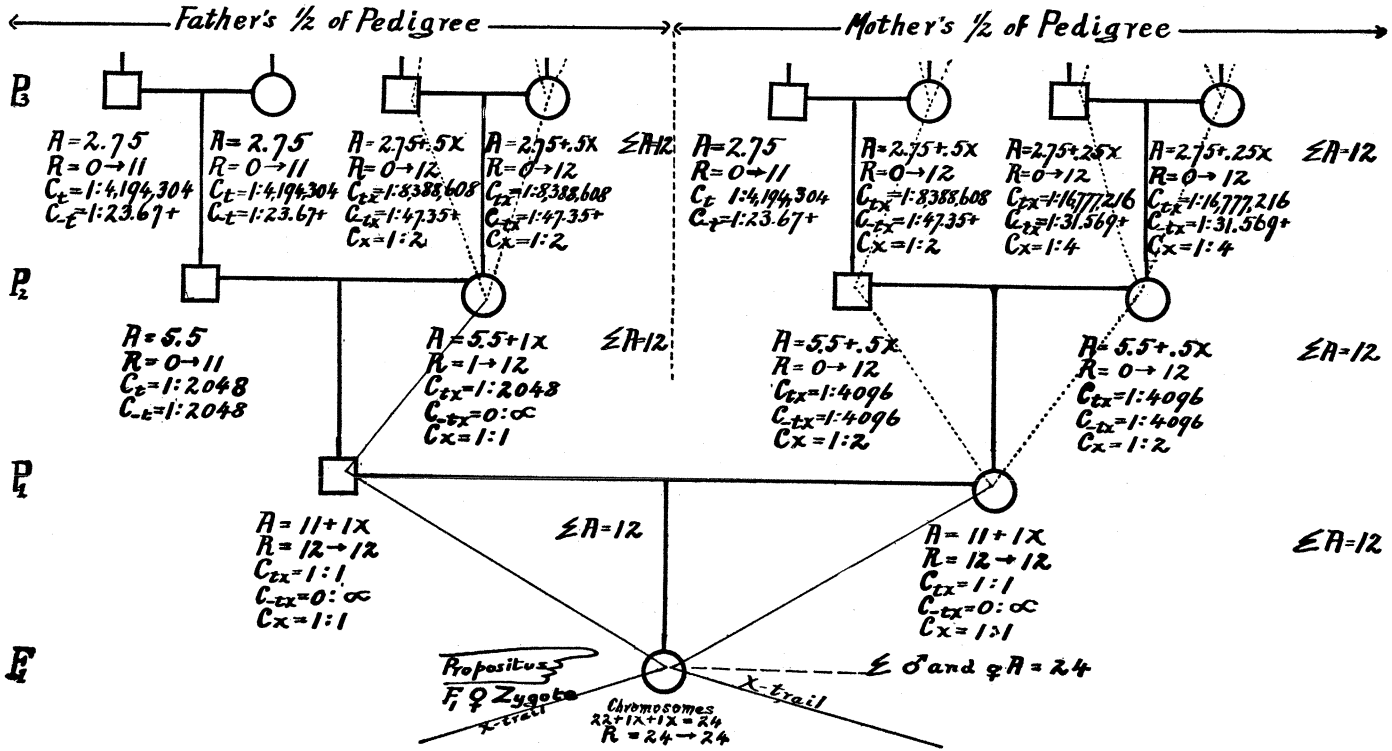
1. Ancestral Influence in the Human Male

based upon average, range and chance in the contribution of chromosomes to the F_1 Zygote.



2. Ancestral Influence in the Human Female

based upon the average, range and chance of contribution of chromosomes to the F_1 Zygote.



to indicate the ancestral or parental generation in relation to F_1. Thus in the great-grandparental generation P_3, $p=3$.

No. 4. C_y = the average number of y-chromosomes contributed to the F_1 zygote by the particular *male* ancestor taken as a type.

No. 1. C_y = the probability that a particular *male* ancestor will contribute the single y-chromosome found in the F_1 *male* zygote.

The value of $1 : C_y$ is always 1 : 1, and it is applicable to the *direct male* line only.

This direct paterial line down which the y-chromosome descends is the so-called "y-trail."

No. 5. C_x = The average number of x-chromosomes contributed to the F_1 zygote by the particular ancestor taken as a type.

$1 : C_x$ = The probability that the particular male or female ancestor will contribute an x-chromosome to the F_1 zygote.

The value of C_x is determined by the following rule:

(*a*) Beginning with the x-chromosomes in the F_1 zygote, without exception (i. e., with the chance of 1 : 1) the *single* x-chromosome in the *male* is derived from his *mother;* and of the *two* x-chromosomes in the *female, one* is derived from *each parent.*

(*b*) In the P_1 and all older generations, in the case of a female zygote the chance of the descent of an x-chromosome from the *father* or *mother* is *equal* (i. e., 1 : 2), but in the *male* the x-chromosome is always received from the *mother* alone (i. e., the chance is 1 : 1).

Therefore, the probability that a given ancestor, taken as a type, will contribute an x-chromosome to the F_1 zygote (i. e., $1 : C_x$), ise qual to the product of all probability ratios, made according to rules (*a*) and (*b*) above, along the x-trail from the selected ancestor to the P_1 generation inclusive.

Thus $1 : C_x$ for the mother's mother's father of a female zygote = $(1 : 1).(1 : 2).(1 : 2) = 1 : 4$; but for the mother's father's mother of a female zygote $1 : C_x = (1 : 1).(1 : 2).(1 : 1) = 1 : 2$.

Thus the so-called "x-trail"—from a *son to the mother only*, but from a *daughter to both the father and mother*, traces the several lines in the ancestral pedigree down *one* of which an x-chromosome *must* descend.

NOTE.—The x-trail and the y-trail and all calculations herein based upon them apply only to those species in which the male is the heterozygous and the female the homozygous sex. In species in which the reverse is true the x- and the y-trails exchange positions. The general rule is that the y-trail follows the heterozygous sex; the x-trail from the homozygous individual to both parents, but from a heterozygous individual to the homozygous parent only.

No. 6. R = Range in number of chromosomes (i. e., in number of single members of chromosome-pairs) possible for the selected ancestor, taken as a type, to contribute to the 24 (i. e., 11 equivalent pairs and 1 xy or 1 xx pair) chromosomes of the F_1 zygote.

In a parent of the P_1 generation, $R = 12 \longrightarrow 12$, i. e., there is no range in the number of chromosomes which the given parent may contribute to the F_1 zygote; this number is always 12. For all ancestors of the P_2 and all older generations, $R = 0 \longrightarrow 11$, except (*a*) for those ancestors from whom an *x*- or a *y*-chromosome *must* certainly descend (solid line *x*-trail or *y*-trail in chart), in whom $R = 1 \longrightarrow 12$; except also (*b*) for those ancestors from whom an *x*-chromosome *may* by alternate chance, descend (dotted line *x*-trail in chart) in whom $R = 0 \longrightarrow 12$.

In a general formula 11 would be substituted for by n, and 12 by $n + 1$, with value as in formula 1.

No. 7. $1 : C_t$ = The probability that *one or the other* member of *each* of *all* of the *equivalent* chromosome-pairs characteristic of the species (i. e., an entire chromosome-series excluding the *xx* and *xy* pairs), from the given ancestor will enter the F_1 zygote.

In the case of ancestors not in the *x*-trail or the *y*-trail, such an occurrence is the extreme limit of ancestral influence possible to a given ancestor, and its happening precludes any hereditary influence at all on the propositus, i. e., the F_1 zygote, on the part of any other ancestor of the same paternal or maternal half-pedigree, as the case may be, except the lineal ancestors and descendants of the given ancestor.

$1 : C_t = 1 : (2^n)^{p-1}$

n = Value as in formula 1. In man n is taken tentatively at 11.

p = Value as in formula 1.

No. 8. $1 : C_{tx}$ or $1 : C_{ty}$ = The probability that *one or the other* member of *each* of the several equivalent chromosome-pairs characteristic of the species, and *also* one *x*- or one *y*-chromosome, as the case may be, from the given ancestor will enter the F_1 zygote. (In man this total gametic number of chromosomes is taken tentatively at 12.)

Such an occurrence can happen only in reference to ancestors in the *x*- or *y*-trails, and its happening precludes any hereditary influence at all on the propositus, i. e., the F_1 zygote, on the part of any other ancestor of the same paternal or maternal half-pedigree, except the lineal ancestors and descendants of the given ancestor.

$1 : C_{tx} = (1 : C_t).(1 : C_x)$

Values of $1 : C_t$ and $1 : C_x$ as in formulas 5 and 7.

$1 : C_{ty} = (1 : C_t).(1 : C_y)$

Values of $1 : C_t$ and $1 : C_y$ as in formulas 4 and 7.

No. 9. $1 : C_{-t}$ = The probability that *no member* of *any* of the equivalent chromosome-pairs characteristic of the species (thus barring for the time being all consideration of the *xx* or *xy* chromosome-pairs) from the given ancestor will enter the F_1 zygote.

In such an occurrence the given ancestor and all of his or her lineal ancestors are *entirely eliminated* as contributors to the natural inheritance of the propositus, i. e., the F_1 zygote, *provided* that such given

ancestor is not in the x-trail or y-trail, and does not, due to inbreeding, appear elsewhere in the ancestral pedigree.

$$1 : C_{-t} = 1 : \left(\frac{2^{p-1}}{2^{p-1} - 1}\right)^n$$

n = Value as in formula 1.

p = Value as in formula 1.

No. 10. $1 : C_{-tx}$ = or $1 : C_{-ty}$ = The probability that no member of any equivalent chromosome-pair, *nor* of the xx or xy chromosome-pair, from the given ancestor will enter the F_1 zygote, i. e., the probability (barring crossing-over and other special phenomena, and the appearance of the given ancestor elsewhere in the pedigree), of the *complete elimination* of the hereditary influence of the given ancestor and all of his or her lineal ancestors, on the propositus, i. e., the F_1 zygote.

This formula is applicable *only* to those ancestors *in the x-trail or y-trail.*

$1 : C_{-tx} = (1 : C_t).(1 : C_{-x})$

$1 : C_{1-y} = (1 : C_{-t}).(1 : C_{-y})$

Values of $1 : C_{-t}$ as in formula 9

$$C_{-x} = \frac{C_x}{C_{x-1}}$$

$$C_{-y} = \frac{C_y}{C_{y-1}}$$

Summary.—The present problem of measuring ancestral influence by tracing chromosomes or gene-s-radical is demonstrated to be a special case under the following general situation:

Given: First. A single unit factor (a gene) in a known situation (in the P_1 generation) and the quotient measuring the probability of its reacting in a definite manner or reaching a definite new situation at the end of a single system of moves or transformations (in the F_1 generation).

Second. The demonstrated synchronization or sequence in the systems of moves or transformations of two or more such unit factors.

By applying the correct principles of combination and chance, the probability that a given complex situation will result from a given set of constituent conditions at the end of a given number of definite kinds of transformations may be mathematically formulated.

In case of measuring ancestral influence by tracing chromosomal descent, the situations and transformations concern definite chromosome-complexes and their breaking-up, their re-combination and their transmission to offspring.

The formulas here set forth are foundational. They are stated in general terms whose validity depends upon their presenting correct mathematical pictures of the chromosomal processes which work out in the germ-cell cycle.